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Total Number of Pages in This Submission	13	**Application Number**	09/775,181
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		First Named Inventor	Donoho
		Group Art Unit	1646
		Examiner Name	R. Li
		Attorney Docket Number	LEX-0129-USA

ENCLOSURES *(check all that apply)*

☐ Fee Transmittal Form	☐ Assignment Papers *(for an Application)*	☐ After Allowance Communication to Group
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PATENT TRADEMARK OFFICE

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm *or* Individual name	Lance K. Ishimoto Reg. No. 41,866 Lexicon Genetics Incorporated
Signature	Lance K Ishimoto by Peter G. Seferian Reg No 40162
Date	April 3, 2002

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THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Donoho *et al.*	Group Art Unit:	1646
Application No.:	09/775,181	Examiner:	R. Li
Filed:	02/01/2001		
Title:	Novel Human Membrane Proteins and Polynucleotides Encoding the Same	Atty. Docket No.	LEX-0129-USA

AMENDMENT AND RESPONSE TO OFFICE ACTION DATED JANUARY 3, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The Applicants acknowledge the receipt of the Office Action ("the Action") mailed on January 3, 2002 (Paper No. 7), which has been carefully reviewed and studied. The Examiner is respectfully requested to enter the following amendments. Reexamination and reconsideration of the application is requested in view of the following amendments and remarks. In order to facilitate the Examiner's evaluation of the application, Applicants have attempted to address the objections and rejections in Paper No.7 in the same order in which they were originally raised.

The response is timely filed and Applicants believe no fees are due in connection with this response. However, the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

AMENDMENT

In the claims:

Please amend claims 1 and 2 so that the text of the amended claims reads as follows:

a1

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

a1 2. (Amended) An isolated nucleic acid molecule comprising a sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

RESPONSE

I. Status of the Claims

Claims 1 and 2 have been amended. No new claims have been added. Claims 1-4 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Amended Claim

Claim 1 has been amended to further clarify the claim, and to recite that the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 1 and SEQ ID NO:1 as originally filed as well as in Section 5.1.

Claim 2 has been amended to further clarify the claim, and to recite highly stringent conditions. Amendment of Claim 2 finds support throughout the specification as originally filed, with particular support and a definition of highly stringent hybridization being found at page 7, lines 21-27.

As the amendments to Claims 1 and 2 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Claim Objection

The Action objects to the sequence listing allegedly because of the lack of adequate description. Although Applicants believe that the sequence listing as originally filed was reasonably clear, in order to further clarify the sequence listing the following information is provided. The nucleic acid of SEQ ID NO 1 encodes the amino acid of SEQ ID NO:2. The nucleic acid of SEQ ID NO 3 encodes the amino acid of SEQ ID NO: 4. The nucleic acid of SEQ ID NO 5 is the nucleic acid sequence of SEQ ID NO:1. with surrounding 5' and 3' regions. Having further clarified the sequence listing, Applicants therefore respectfully request that the objection to the sequence listing be withdrawn.

IV. Rejection of Claims 1-4 Under 35 U.S.C. § 101

The Action rejects claims 1-4 under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities. As taught in the application and as well known to those of skill in the art, G protein coupled receptors (GPCRs) play a critical role in, *intra alia*, signal transduction and cell activation. In fact, many oncogenes are linked to GPCRs and GPCRs are the target of many pharmaceuticals. Therefore, the identification of a new and novel human GPCR has great utility.

The first issue raised in the Action is that it is unclear that the present invention is a GPCR. Included in the Action's reasons for the alleged lack of utility is the statement that "the disclosure does not provide any experimental data or information on whether the claimed proteins actually function like GPCRs (Action at page 3). However, this emphasis is misplaced as it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962). Applicants assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the

burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants asserted utility. Given that over half of the current drugs on the market address GPCR proteins, there can be no question that those skilled in the art recognize the pharmaceutical utility of GPCR proteins.

The Action also states (page 3, line 3-6) that based on a quote, that appears in a single non-peer reviewed "news" article, that "The state of the art in protein science indicates that it is impossible to predict protein functions solely with structure homology. "Identical structural features, or folds, in proteins can perform many different roles and so using only homology to predict function is a "very dangerous and difficult mission" (Apoorva Mandavilli, *Protein folds shield different roles*, BiomMednet News, November 1, 2001: internal quote from Janet Thornton). However, later in the very same article the same woman is noted to have said that "Function is also likely to change once sequence identity dips below 40%". This strongly suggests that Janet Thornton believes that once sequence identity dips below 40%, predicting protein function becomes less reliable (stated, rather dramatically, as a "very dangerous and difficult mission").

While prediction of protein function below the 40% sequence identity level may well be a tricky task, Applicants do not agree that in general the state of the art in protein science indicates that it is impossible to predict protein functions based solely on structural homology, particularly when such homology is significantly greater than 40%. The prediction of function based on the presence of functional domains is well recognized by those of skill in the art. Therefore, it is the Applicants' position that those of skill in the art would find our assertion that the present invention is a GPCR to be credible. In the present instance, the specification teaches that the described sequences display the 7 hydrophobic transmembrane regions that are characteristic of GPCR proteins, and that the described sequences share further structural domains characteristic of other GPCRs. To rebut the clear teaching in the specification, the Examiner has made no evidence of record that refutes the teaching in the specification.

Additionally, methods similar to those of the present invention were used to identify the GPCR of issued U.S. Patent 6,043,052. Issued U.S. Patents are presumed to be valid and to meet the requirements of 35 U.S.C. §§ 101, 102, 103 and 112, specifically, that they have utility, are novel, non-obvious, are enabled, meet the written description requirements and particularly point out and distinctly claim the invention. Therefore, the Applicants' assertion that the described GPCR is in fact a GPCR is supported by issued U.S. Patent 6,043,052, as well as the plethora of other GPCR patents that the office has issued. For example, the specific and substantial utility of human GPCRs is evidenced by the fact that they are the subject of the above mentioned U.S. Patent No. 6,043,052 which discloses polynucleotides encoding a novel GPCR and U.S. Patent Nos. 5,891,646 and 6,110,693, both of which disclose and claim methods for detecting GPCR activity *in vivo* and *in vitro*, methods for assaying GPCR activity, and methods of screening for GPCR ligands, GPCR kinase activity, components that interact with GPCR regulatory processes and constructs useful in such methods. The issuance of these U.S. patents clearly indicates that GPCR polynucleotides have utility and that such utilities were sufficiently specific and substantial to warrant the issuance of U.S. patents directed to methods used to identify and characterize GPCRs. The teachings of these patentable disclosures are directly applicable to the present invention (GPCR polynucleotides) and are evidence that those skilled in the art recognize the specific and substantial utility of GPCRs. In light of the issuance of U.S. Patent No. 6,043,052 on polynucleotides encoding a novel GPCR, Applicants respectfully submit that the present application, which also describes polynucleotides encoding a novel GPCR, describes an invention with specific and substantial utility fully compliant with 35 U.S.C. § 101.

Although the above discussion is believed to be dispositive of the utility issue, the Applicants would like to further direct the Examiner's attention to the parts of the specification (Sections 5.0 and 5.1) that describe the use of sequences in a gene chip format to provide a high throughput analysis of the relevant cellular "transcriptome".

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. The sequences of the present invention describe a novel gene encoding a GPCR and provide a unique identifier of the corresponding gene. Such gene chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, such as U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. The present nucleotide sequences clearly encode human GPCRs, as detailed throughout the specification. The specification also teaches that GPCRs are associated with a wide variety of cellular functions, and as such, that GPCR interacting proteins have been subject to intense scrutiny as potential drug targets. Therefore, as the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such gene chips.

The Examiner is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in

general, in the time and resources that are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such gene chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Moreover, the presently described novel GPCRs provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Yet another example of the utility of the present invention is in expanding the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise. Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (C.C.P.A. 1964); *In re Malachowski*, 189 USPQ 432 (C.C.P.A. 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed

polynucleotides, the Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons that in-turn encode polypeptide sequences. The presently described cDNAs provide biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the described cDNA sequences define which exons are actually spliced together to produce an active transcript (*i.e.*, such sequences are generally required to conclusively identify functional exon splice-junctions). The Applicants submit that one skilled in the art would have clearly understood that the above *substantial and specific* utilities as inherent features of the presently described sequences.

For the many reasons described above, the present invention clearly has specific, substantial, credible and well established utility. Therefore, Applicants submit that the rejection of Claims 1-4 under 35 U.S.C. § 101 has been overcome and the Examiner is respectfully requested to withdraw the pending rejection of Claims 1-4 under 35 U.S.C. § 101.

V. Rejection of Claims 1-4 Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-4 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-4 have been shown to have a specific, substantial, credible and well established utility, as detailed in section IV above. Applicants therefore respectfully request that the rejection of claims 1-4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

In addition, Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph as reciting a genus of polynucleotides of any size that has at least 22 contiguous nucleotides of SEQ ID NO: 1. While

Applicants do not agree with the Action's position, the rejection of Claim 1 under 35 U.S.C. § 112, first paragraph has been avoided by Applicants' amendment of Claim 1. Accordingly, the Examiner is respectfully requested to withdraw the pending rejection of Claim 1 under 35 U.S.C. § 112, first paragraph.

VI. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term " hybridizes under stringent conditions". Although Applicants believe that this claim as originally filed sufficiently points out and distinctly claims the invention, in order to more rapidly progress the case to allowance, Applicants have amended Claim 2 to specify "highly" stringent conditions. Highly stringent conditions for full length molecules are defined in the specification on page 7, lines 21-27. Applicants respectfully submit that this rejection has thus been avoided by Applicant's amendment of Claim 2 to specify "highly" stringent conditions. Accordingly, the Examiner is respectfully requested to withdraw the pending rejection of Claim 2 under 35 U.S.C. § 112, second paragraph.

VII. Rejection of Claim 1 Under 35 U.S.C. § 102(a)

Claim 1 stands rejected under 35 U.S.C. § 102(a), as allegedly anticipated by Ohara et al., (IDS, paper 6, GenBank accession number AB032962, January, 2000 "NCI-CGAP"). While Applicants do not necessarily agree with the present rejection, as Claim 1 has been amended to recite the full length of the nucleotide sequence of SEQ ID NO:1, Applicants submit that the rejection of Claim 1 under 35 U.S.C. § 102(a) has been thus avoided and respectfully request withdrawal of the pending rejection of claim 1 under 35 U.S.C. § 102(a).

VIII. Conclusion

The present document is a full and complete response to the

Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

April 3, 2002
Date

Peter G. Seferian
Lance K Ishimoto by [signature] Reg No 40,162
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Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/775,181

1. (Amended) An isolated nucleic acid molecule comprising [at least 22 contiguous bases of] the nucleotide sequence [first disclosed in] of SEQ ID NO:1.

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:1 or the complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

4. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.